The ocular signs and complications of epidermolysis bullosa

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Summary

Eleven patients with the dystrophic form of epidermolysis bullosa underwent ophthalmic assessment to establish the presence, characteristics, and extent of any ocular involvement. Eight patients were found to have eye changes: these included varying degrees of symblepharon, broadening of the limbus, and corneal opacities. Taken as a group, these changes formed a characteristic pattern. The majority of patients were asymptomatic and the ocular changes appear to be only slowly progressive. Recurrent corneal abrasion and symblepharon are the most important complications.

Introduction

Epidermolysis bullosa is a collective term for a group of rare hereditary skin diseases which are all characterized by the tendency to blister formation after minor degrees of trauma. There are many different types of epidermolysis bullosa and the most useful classification is based on the level in the skin at which the blister develops (Figure 1). In this scheme there are three main groups:

(1) Epidermolysis bullosa simplex, where the blister develops within the basal epidermal cells.

(2) Junctional epidermolysis bullosa, where the cleavage occurs in the superficial lamina lucida layer of the epidermal basement membrane.

(3) Dystrophic epidermolysis bullosa where the separation occurs at the level of the lamina densa and anchoring fibrils in the epidermal basement membrane.

All these three types are inherited in a simple Mendelian fashion: epidermolysis bullosa simplex is dominant, junctional epidermolysis bullosa is recessive, and dystrophic epidermolysis bullosa may be either dominant or recessive.

Ocular complications have been reported in most variants of epidermolysis bullosa[1,2], but the dystrophic form is the most severe and most frequently involves the eyes and we have concentrated on this group in the study.

The blisters of the dystrophic form cause permanent scarring and the clinical picture shows a wide variation from patient to patient with the recessive disease being more common and more severe than the dominant variety.

Patients with mild dystrophic disease tend to have a normal early childhood with normal development of hands, feet, nails, and teeth. They present in middle to late childhood with recurrent blistering and mild scar formation after trauma. The general health of these patients is not affected and they lead a relatively normal life. This group have a low incidence of ocular problems.

Severe dystrophic disease is disabling and cosmetically disfiguring. In these patients the blisters often appear shortly after birth and extensive skin loss may endanger the life of the baby. If the neonatal period is survived then the recurrent blister formation causes severe scarring of the skin, and mucosal surfaces. This results in disabling deformities of the hands and feet with destruction of the nails, and fusion together of the fingers and toes (Figure 2).

There is often involvement of the mouth with scarring of the buccal mucosa and abnormal development of the teeth which tend to be discoloured and uneven, and some patients develop oesophageal strictures.

This group have a higher incidence of ocular involvement. Because of their multiple problems these children are usually small for their age and are always unfortunately at risk of developing a fatal septicaemia because of the very extensive blistering. The slightest trauma can result in a blister in these children, and particular care must be taken during the eye examination: it is easy to knock the chin or nose on the slit-lamp and even attempts to evert the lids can result in blister formation. If the child requires surgery or an examination under anaesthetic great care must be taken not to traumatize the face and eyelids with the mask, or larynx during the administration of the anaesthetic.

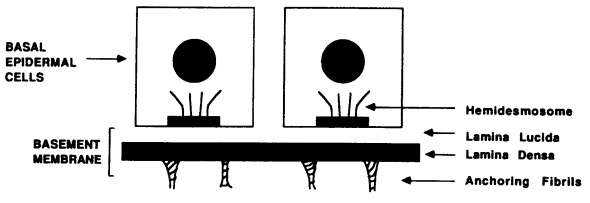

Figure 1. Diagram of the ultrastructure of the epidermal basement membrane

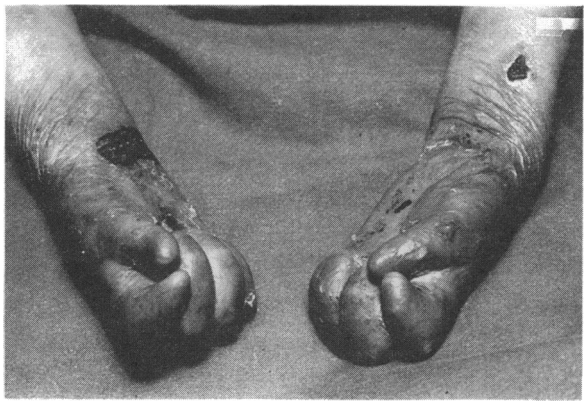

Figure 2. The hands of a child with severe dystrophic disease showing fusion of the fingers

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Patients and methods

Eleven patients with dystrophic epidermolysis bullosa were reviewed at St Thomas's Hospital between May 1986 and May 1987. These patients were under the care of the Department of Plastic Surgery or the Institute of Dermatology. Their mean age was 14 years with a range of 5 weeks to 55 years; there were 8 males and 3 females. All the patients had a full ophthalmic assessment which included slit-lamp examination except for the 5-week-old baby. Any history of eye problems in the past or present was noted, and special attention was directed to the appearance of the lids, conjunctiva and cornea. Three of the patients were examined on more than one occasion.

The results of the assessment were entered on a proforma which recorded details of the type of inheritance, degree of skin involvement, ocular history, and results of the eye examination.

Results

Eight of the 11 patients examined had some sign of ocular involvement, representing 73% of all patients examined. Three of the 8 patients gave a history of ocular problems and the rest were asymptomatic. Two of the 3 had symptoms of recurrent erosions in the past, and one of the 3 had symptoms of intermittent conjunctivitis and blepharitis and had also had surgery to a symblepharon the previous year at another hospital.

On examination there were three main findings:

(1) Symblepharon (Figure 3). This was present in 6 of the 8 patients. The amount of symblepharon varied from a very mild localized change often at the medial or lateral canthal region, to severe symblepharon joining the lid margin to the peripheral cornea. One patient had developed slowly progressing fleshy vascular membranes in both eyes which were spreading from the inferior conjunctival fornix up over the inferior cornea. The membrane on the left cornea was excised at another hospital but recurred more extensively soon after surgery (Figure 4). The patient's vision is still normal and he remains asymptomatic.

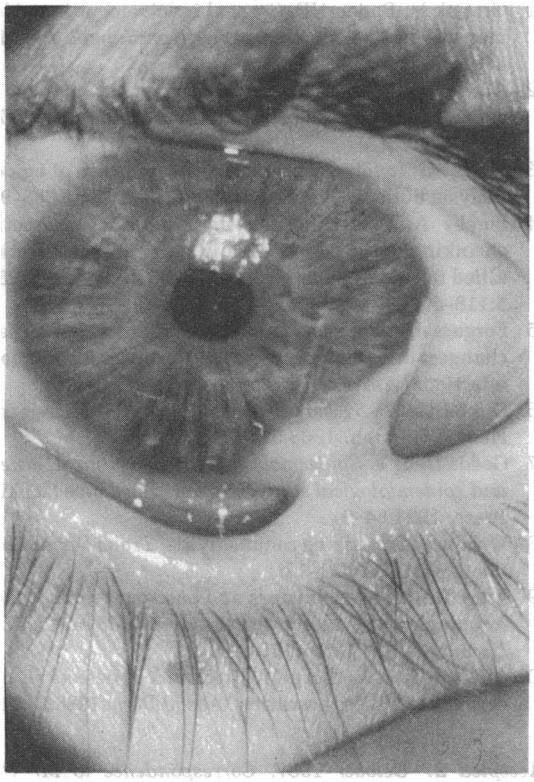

Figure 3. A large symblepharon joining the lid margin to the inferior cornea

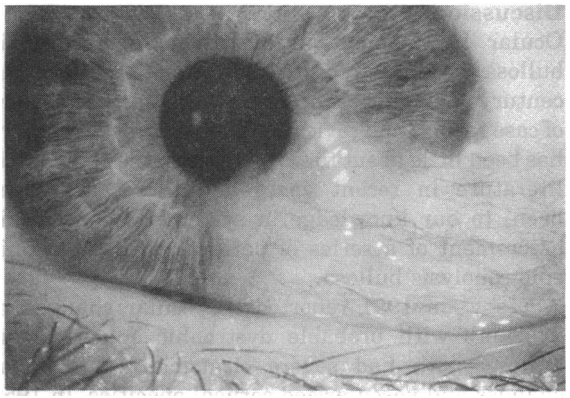

Figure 4. Fleshy vascular membrane spreading over the inferior cornea

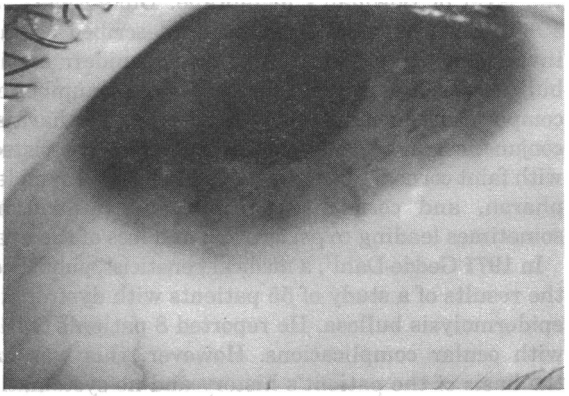

Figure 5. An area of limbal broadening affecting the inferior limbus

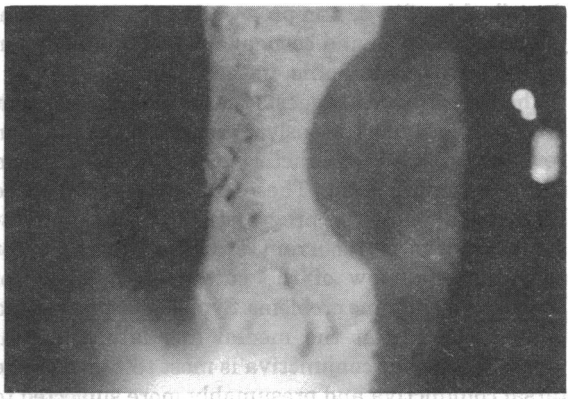

Figure 6. Reticular opacity in the region of Bowman's membrane in the central part of the cornea

(2) Limbal broadening (Figure 5). Five patients had an avascular broadening of the superior and inferior limbus. This change appeared to be asymptomatic.

(3) Corneal opacity (Figure 6). Two patients were found to have a distinctive reticular pattern of stromal opacity at the level of Bowman's membrane. The reticular change was in the central cornea but did not affect vision. Both these patients had recently had symptoms of recurrent erosion.

Only 3 patients required any treatment: 2 patients needed chloramphenicol eye ointment and eye padding for symptomatic relief of corneal abrasion, and one patient developed a meibomian cyst which was incised and curetted.

Discussion

Ocular involvement in dystrophic epidermolysis bullosa was first reported at the beginning of the century[3] and since then there have been a number of case reports and reviews published. However, there has been little about these patients in the ophthalmic literature in recent years and there has never been, to our knowledge, a systematic ophthalmic assessment of a series of patients with dystrophic epidermolysis bullosa.

Sorsby[4] in 1951 reported the ocular changes in 2 sisters with probable dystrophic epidermolysis bullosa: both had severe cicatricial conjunctival changes and vascularized corneal opacities. In 1959 Forgacs and Franceschetti[5] published a report of a girl with dystrophic epidermolysis bullosa who had a diffuse granular clouding of the cornea at the level of Bowman's membrane. Duke-Elder[6] in 1965 reviewed the literature and described ocular involvement in the dystrophic type of epidermolysis bullosa as comparatively rare. He noted a number of complications including conjunctivitis and blepharitis, conjunctival and corneal vesicles (sometimes associated with faint corneal scars), cicatricial bands and symblepharon, and corneal ulceration and infiltration sometimes leading to perforation and loss of the eye.

In 1971 Gedde-Dahl[7], a medical geneticist, published the results of a study of 55 patients with dystrophic epidermolysis bullosa. He reported 8 patients (14%) with ocular complications. However, this was on the basis of the patient's history and no systematic ophthalmic examination was performed. Recurrent corneal erosions and keratoconjunctivitis were the commonest features. More recently Wright[8] in 1986 described localized, non-progressive cicatrizing conjunctival changes and corneal epithelial erosions in patients with dystrophic disease.

The present study suggests that ocular involvement is commoner than previously reported and examination reveals a range of characteristic changes visible in the anterior segment. These changes tended to be localized and slowly progressive. The commonest symptom was of recurrent erosions, which is not surprising in view of the cutaneous evidence of basement membrane problems. Symblepharon occurred most commonly at the medial and lateral canthi where the bulbar conjunctiva is most tethered to the tarsal conjunctiva and presumably more subjected to stretching by horizontal eye movements. Our findings are similar to previous reports except for the reticular opacity in the cornea in 2 patients and the presence of limbal broadening in 5 patients.

The exact mechanism of these ocular changes is still unknown but recent developments in the understanding of the basic defect in dystrophic epidermolysis bullosa raises some intriguing possibilities. Within the past 5 years a range of monoclonal antibody probes have been developed which bind with normal components of the epidermal basement membrane[9].

For example the monoclonal antibody LH 7:2 is specific for a component of the lamina densa and an immunofluorescence micrograph of normal skin would show labelling of the lamina densa by the antibody.

However, patients with dystrophic epidermolysis bullosa have been found to be deficient in certain basement membrane components and the antibody LH 7:2 fails to label the lamina densa in skin biopsies of these patients. Other antibodies which are specific for antigens in the anchoring fibrils also fail to label skin biopsies from these patients.

Apart from reduced amounts or absence of normal basement membrane components there have been reports of abnormal substances in the region of the basement membrane. A number of workers have demonstrated high amounts of a mutant collagenase being synthesized by dermal fibroblasts from dystrophic epidermolysis bullosa patients[10].

Although no studies have yet been published on the labelling of conjunctival and corneal basement membrane of patients with dystrophic disease using these monoclonal antibody probes, it would seem reasonable to assume that these basement membranes are also deficient in certain normal components. There may also be raised levels of abnormal collagenase in the sub-conjunctival connective tissue and the corneal stroma.

These abnormalities must in some way lead to a type of modified blister formation in the conjunctiva and cornea: the conjunctiva develops symblepharon and the cornea develops recurrent erosions and subepithelial scarring.

Conclusion

We have presented a series of patients with dystrophic epidermolysis bullosa who underwent a systematic ophthalmic assessment. Ocular involvement was found in more than 70% of cases, although most patients were asymptomatic. Recent developments in the biochemistry and immunohistochemistry of the basic defect in dystrophic epidermolysis bullosa may soon elucidate the mechanisms of the ocular changes.

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